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Transdermal anastrozole patch formulation and *in vitro* release study

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ABSTRACT

Anastrozole is commonly prescribed to postmenopausal women with hormone-sensitive breast cancer; however, its severe side effects – often dependent on dosage – are frequently linked to the standard oral formulation. A sustained-release transdermal delivery system may offer a means of mitigating these adverse effects. In this study, transdermal patches containing anastrozole were developed, and the influence of polymer composition on the drug's *in vitro* release profile was evaluated. Polyethylene glycol 400 (PEG 400) served as a plasticizer, with varying ratios of hydrophobic to hydrophilic polymers: Eudragit L-100 and hydroxypropyl methylcellulose (HPMC), respectively. The formulations were assessed for their physicochemical properties and their *in vitro* drug release in phosphate-buffered solution (pH 7.4) at 32.0°C ± 1.0°C. Among these, the formulation containing a 7:3 Eudragit L-100 to HPMC ratio was selected, as its release kinetics conformed to the Higuchi model, thereby suggesting diffusion as the predominant mechanism of sustained drug release.

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1. Introduction

Breast cancer remains the leading cause of mortality and the most pressing reproductive health concern among women aged over 15. Third-generation nonsteroidal aromatase inhibitors, such as anastrozole, are approved for the treatment of breast cancer. Currently, the only available form of anastrozole is an orally administered, immediate-release formulation, which is frequently associated with serious systemic side effects[1]. In contrast, a controlled-release transdermal formulation of anastrozole could offer several potential advantages, including prolonged pharmacological action due to sustained release, maintenance of

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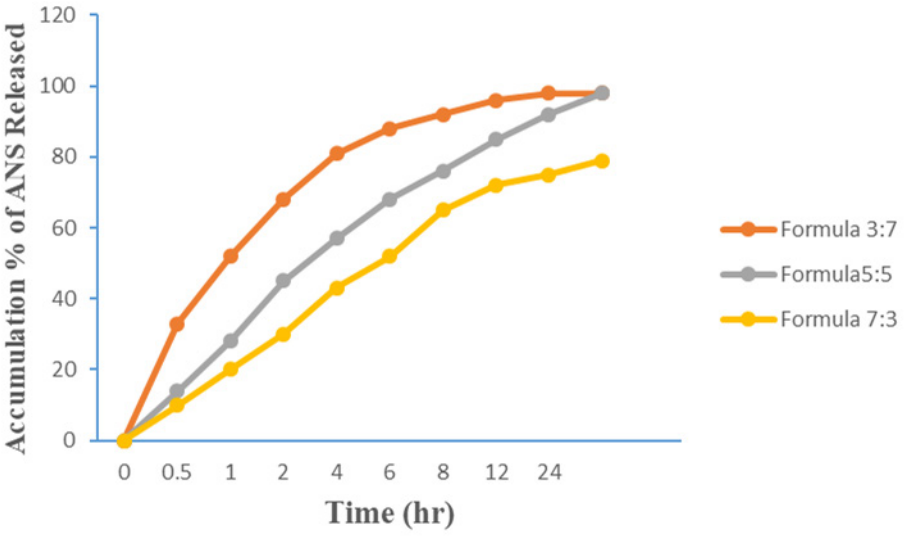

Figure 1. *In vitro drug release (%) from anastrozole-loaded transdermal patches prepared with varying ratios of Eudragit L-100 to hydroxypropyl methylcellulose (HPMC): 7:3, 5:5, and 3:7. Notes: results are presented as mean ± standard deviation (SD); n=3.*

stable, therapeutically effective drug concentrations, avoidance of undesirable plasma peak fluctuations, and improved patient compliance[2]. Accordingly, the present study aimed at developing transdermal anastrozole patches and at assessing the influence of polymer ratios on the drug's *in vitro* release profile.

2. Methodology

2.1. Materials and transdermal adhesive patch preparation

Anastrozole was procured from HyperChem® (Zhejiang, China), and all polymers and solvents were supplied by the Pioneer Company. The transdermal patches were prepared using a solvent-casting technique. A polymeric solution was created by dissolving varying ratios of Eudragit L-100 to hydroxypropyl methylcellulose (HPMC) at ratios 7:3, 5:5, and 3:7, in 15 mL of ethanol and water, followed by stirring for 30 min at 250 rpm using a hot plate magnetic stirrer. Polyethylene glycol 400 (PEG 400; 30% w/w) was incorporated as a plasticizer. Separately, 1 mg of anastrozole was dissolved in 5 mL of methanol and was added to the polymer solution. The combined mixture was sonicated for 20 min at 35°C in order to remove residual air bubbles. The resulting solution was poured onto a petri dish lined with a 5% w/v polyvinyl alcohol (PVA) backing layer. An inverted funnel was placed above the dish so as to regulate evaporation, and the solvent was allowed to evaporate at ambient temperature over 24 h[2].

2.2. Assessment of the transdermal patches

2.2.1. Weight and thickness measurement

Each of the three formulations was weighed using a digital scale, and both mean weight and standard deviation (SD) were calculated[3]. Patch thickness was measured using a vernier caliper (n=3), and the mean thickness with SD was recorded[2].

2.2.2. Swelling index and percentage of weight change[4]

Three 1×1-cm film samples were pre-weighed and placed in petri dishes containing distilled water. Weights were recorded at predetermined intervals. Swelling behavior was quantified using the formulas:

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$$swelling\ index = (W_2 - W_1)/W_1$$

$$swelling\text{-}induced\ weight\ gain\ (\%) = [(W_2 - W_1)/W_1] \times 100$$

where W_1 is the initial weight of the film, and W_2 is the weight at time t. After 60 min, the erosion was calculated as:

$$erosion\text{-}induced\ weight\ loss\ (\%) = [(W_1 - W_2)/W_1] \times 100$$

2.2.3. Content uniformity test[5]

A 2×2-cm film sample (in triplicate for each formulation) was dissolved in 100 mL of phosphate buffer (pH 7.4) using a magnetic stirrer at 32°C. A 3-mL aliquot was filtered through a syringe filter and diluted with an equal volume of fresh buffer. Drug concentration was measured by UV spectrophotometry at 215 nm, and quantified using a calibration curve.

2.2.4. Drug release study[5]

In vitro release studies (n=3) were performed using a USP apparatus containing 200 mL of phosphate buffer (pH 7.4), maintained at 32.0°C ± 1.0°C with constant agitation at 50 rpm. Samples of 3 mL were withdrawn at regular intervals over 24 h and were analysed spectrophotometrically at 215 nm.

2.2.5. Drug release kinetic modelling[5]

The release kinetics of anastrozole from the patches were assessed using mathematical models following the *in vitro* release experiments.

3. Results and Discussion

The transdermal patches developed in this study exhibited weights ranging from 1.50 ± 0.011 to 1.60 ± 0.013 g. Weight variation within each formulation was minimal and consistent, as evidenced by the low standard deviation values. The relatively higher patch weight is attributable to the presence of a backing layer[6]. On the other hand, patch thickness ranged from 0.66 ± 0.013 cm to 0.69 ± 0.012 cm; the narrow range and low standard deviations suggest that the fabrication method produced reproducible films[6].

Among the formulations, the 7:3 Eudragit L-100 to HPMC ratio displayed the lowest swelling index and percentage weight gain (0.91 and 80.69%, respectively), while the 3:7 ratio yielded the highest values (1.70 and 125.74%, respectively), consistent with its elevated hydrophilic polymer content. When immersed in water, the swelling index reflects the extent of hydration within the film. Excess hydration may create voids within the polymer matrix, which could affect the sustained-release profile. Additionally, excessive swelling can compromise the patch's mechanical stability[6].

Erosion and disintegration profiles following 60 min of water immersion revealed that the increased Eudragit L-100 content – owing to its hydrophobic nature – was associated with reduced disintegration[7]. The 7:3 formulation exhibited the lowest erosion rate at 2.25%.

Drug content across all assessed formulations was highly consistent (100.06% ± 0.02%, 98.20% ± 0.08%, and 99.78% ± 0.04%), as indicated by minimal standard deviation values. Uniform drug distribution within the matrix is a critical feature of sustained-release systems, supporting predictable pharmacokinetics[8].

Figure 1 illustrates that patches with higher HPMC content exhibited a pronounced burst release effect, whereas the 7:3 formulation had the lowest burst release among all tested variants. This trend reflects the role of the hydrophobic polymer composition in moderating drug release. A reduction in the initial burst and an enhancement of the sustained-release behavior were achieved by increasing the hydrophobic fraction and by reducing the hydrophilic polymer content in the matrix[9]. Finally, the release kinetics of the 7:3 formulation demonstrated optimal fit with the Higuchi model (correlation coefficient $R^2 = 0.9821$), thereby indicating that diffusion was the dominant mechanism governing drug release from the matrix[10].

4. Conclusion

The findings of this study support the development of a sustained-release transdermal patch containing anastrozole using a 7:3 Eudragit L-100 to HPMC ratio. As the proportion of HPMC increases, drug release is accelerated, whereas Eudragit L-100 demonstrates retardant properties at higher concentrations. This polymer combination facilitates a sustained release of

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anastrozole *via* diffusion-driven kinetics, and may offer a viable alternative to existing oral formulations.

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Conflicts of interest

None exist.

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